recognition target (FRT) site on one end and a modified heterospecific FRT site on the other end for tagging,

b) selecting cell clones surviving the conditions for positive selection,

c) exchanging said first DNA expression cassette against an incoming second DNA expression cassette located on a circular vector and carrying a homologous or heterologous gene (transgene) of any coding sequence flanked by the same FRT sites as said first DNA expression cassette mediated by the action of FLP-recombinase,

wherein said cells are vertebrate cells which can regenerate to complete organisms, and said parts of cells are nuclei of vertebrate cells, which can be inserted into regenerative cells, and wherein

d) maintaining the conditions for positive selection during cultivation of said cells obtained in step b) while exchanging said first DNA expression cassette against said incoming second DNA expression cassette.

e) using in step c) an incoming second DNA expression cassette which is marker-free, and

f) selecting cell clones obtained after step c) surviving the conditions for negative selection.

B1

B2

3. (Amended) The method according to claim 1 wherein said modified heterospecific FRT site is a FRT spacer mutant.

B3

5. (Amended) The method of claim 1 wherein said vertebrate cells which can be regenerated are vertebrate embryonic stem (ES) cells.

B4

7. (Amended) Regenerative vertebrate cells comprising a modified genome obtainable by the method of claim 1.